Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the Claims

1-274. (Canceled)

275. (Currently Amended) A method for enzymatically modifying a conjugate comprising the steps of:

providing a conjugate comprising a nucleic acid and a synthetic binding unit, wherein the synthetic binding unit is selected from the group consisting of pRNA, pDNA, and CNA; and

contacting the conjugate with at least one enzyme to effect modification of the nucleic acid,

wherein when the synthetic binding unit is pRNA or pDNA, the synthetic binding unit and the nucleic acid are connected via a linkage selected from the group consisting of the 2' end of the synthetic binding unit to the 5' end of the nucleic acid, 2' end of the synthetic binding unit to the 3' end of the nucleic acid, 4' end of the synthetic binding unit to the 5' end of the nucleic acid, and 4' end of the synthetic binding unit to the 3' end of the nucleic acid.

276. (Previously Presented) The method of claim 275, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the other reagents include a nucleic acid which hybridizes to the NA of the conjugate.

277. (Previously Presented) The method of claim 275, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the other reagents include nucleoside triphosphates or modified nucleoside triphosphates.

278. (Previously Presented) The method of claim 275, wherein the at least one enzyme is selected from the group consisting of a polymerase, a ligase, an endonuclease, an

exonuclease, a kinase, a methyltransferase, a methylase, a restriction endonuclease, and a terminal transferase.

279. (Previously Presented) The method of claim 275, wherein the at least one enzyme is a ligase, and the nucleic acid of the conjugate is modified by ligation of a terminus of the nucleic acid to at least one additional nucleic acid.

280. (Previously Presented) The method of claim 279, wherein the ligation is template-dependent, and wherein the nucleic acid of the conjugate and the at least one additional nucleic acid are hybridized to adjacent sequences of a template nucleic acid.

281. (Previously Presented) The method of claim 279, wherein the ligation is template-independent, and wherein the nucleic acid of the conjugate and the at least one additional nucleic acid are single stranded.

282. (Previously Presented) The method of claim 281, wherein the ligase used is a T4 RNA ligase.

283. (Previously Presented) The method of claim 279, wherein the ligation is a blunt-end, and wherein the nucleic acid of the conjugate and the at least one additional nucleic acid are double stranded.

284. (Previously Presented) The method of claim 275, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a polymerase, wherein the nucleic acid of the conjugate has an unblocked 3' terminus, wherein the other reagents comprise a template nucleic acid to which the unblocked 3' terminus of the nucleic acid hybridizes, and wherein the nucleic acid is modified by the addition of at least one nucleoside complementary to the template nucleic acid to the 3' terminus of the nucleic acid.

285. (Previously Presented) The method of claim 284, further comprising the step of adding a dideoxynucleotide to the nucleic acid of the conjugate.

286. (Previously Presented) The method of claim 284, further comprising the step of adding a labeled nucleotide to the nucleic acid of the conjugate.

287. (Previously Presented) The method of claim 284 wherein the template nucleic acid is derived from a biological sample.

288. (Previously Presented) The method of claim 287 wherein the biological sample is derived from a sample selected from the group consisting of human materials, animal materials, plant materials, fungal materials, cell cultures, viral cultures, food samples, and water samples.

289. (Previously Presented) The method of claim 284 wherein the polymerase is at least one enzyme selected from the group consisting of DNA polymerases, RNA polymerases, and reverse transcriptases.

290. (Previously Presented) The method of claim 284 wherein at least a portion of the template nucleic acid sequence is amplified.

291. (Previously Presented) The method of claim 284, wherein the polymerase is a thermostable polymerase, and wherein the step of contacting the conjugate with at least one enzyme comprise thermocycling the conjugate and the at least one enzyme to alternately i) dissociate extension products from the template nucleic acid and ii) allow the hybridization of conjugate nucleic acid to the template and enzymatic extension of the nucleic acid of the conjugate, wherein at least a portion of the template nucleic acid sequence is amplified.

292. (Previously Presented) The method of claim 284, further comprising contacting the conjugate with a restriction endonuclease, wherein the nucleic acid of the conjugate comprises an endonuclease recognition sequence 5' of the 3' terminus which hybridizes to the template nucleic acid, and wherein at least a portion of the template nucleic acid sequence is amplified by strand displacement amplification.

293. (Previously Presented) The method of claim 284, wherein the polymerase is a mixture of an RNA polymerase and a reverse transcriptase, further comprising contacting the conjugate with a RNAase H enzyme, wherein at least a portion of the template nucleic acid sequence is amplified by transcription mediated amplification.

294. (Previously Presented) The method of claim 275, wherein the enzyme is a terminal transferase, and the nucleic acid of the conjugate is modified by addition of at least one nucleoside to the 3' terminus of the nucleic acid.

295. (Previously Presented) The method of claim 294, further comprising the step of adding a labeled nucleoside to the nucleic acid of the conjugate.

296. (Previously Presented) The method of claim 294, wherein a homopolymeric tail is added to the nucleic acid of the conjugate.

297. (Previously Presented) The method of claim 275, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the nucleic acid of the conjugate and the target nucleic acid are cleaved by the restriction endonuclease.

298. (Previously Presented) The method of claim 275, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the nucleic acid of the conjugate but not the target nucleic acid is cleaved by the restriction endonuclease.

299. (Previously Presented) The method of claim 275, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the target nucleic acid but not the nucleic acid of the conjugate is cleaved by the restriction endonuclease.

300. (Previously Presented) The method of claim 275, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the enzyme is a RNAse H, wherein the other reagents comprise an RNA target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the target RNA nucleic acid hybridizing to the nucleic acid of the conjugate is degraded by the RNAse.

301. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is within 30 nucleotides of the attachment point.

302. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is within 20 nucleotides of the attachment point.

303. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is within 15 nucleotides of the attachment point.

304. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is within 10 nucleotides of the attachment point.

305. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is within 7 nucleotides of the attachment point.

306. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is within 5 nucleotides of the attachment point.

307. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is within 2 nucleotides of the attachment point.

308. (Previously Presented) The method of claim 275, wherein the nucleic acid and the synthetic binding unit are joined at an attachment point, wherein the enzymatic modification is the nucleotide at the attachment point.

309-318. (Canceled)

319. (Previously Presented) The method of claim 275, wherein the nucleic acid is selected from the group consisting of deoxyribonucleic acids, ribonucleic acids, and chemically modified nucleic acids.

320. (Previously Presented) The method of claim 275, wherein the nucleic acid is selected from the group consisting of phosphorothioate nucleic acids, phosphorodithioate nucleic acids, methylphosphonate nucleic acids, 2'-O-methyl RNA, and 2'-fluoro RNA.

321. (Previously Presented) The method of claim 275, wherein the nucleic acid is selected from the group consisting of peptide nucleic acids (PNA) and locked nucleic acids (LNA.)

322. (Previously Presented) The method of claim 275, wherein the nucleic acid is selected from the group consisting of an aptamer and an aptazyme.

323. (Previously Presented) The method of claim 275, wherein the conjugate further comprises at least one labeling moiety.

324. (Previously Presented) The method of claim 323, wherein the at least one labeling moiety is selected from the group consisting of fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, micro-particles, paramagnetic micro-particles, and enzymatic labeling moieties.

325. (Previously Presented) The method of claim 323, wherein the labeling moiety is a fluorescent dye moiety selected from the group consisting of: boron dipyrromethane difluoride dyes, cyanine dyes, fluorescein dyes, rhodamine dyes, phycoerythrin dyes, coumarin dyes, Texas Red dyes, green dyes, FAM, HEX, TET, TAMRA, ROX, EDANA, 4-Acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid, 4,4'-Diisothiocyanatostilbene-2,2'-disulfonic acid, Succinimidyl pyrene butyrate, Acridine isothiocyanate, Cascade Blue, Oregon Green, Lucifer Yellow vinyl sulfone, and IR1446.

326. (Previously Presented) The method of claim 323, wherein the labeling moiety is a quencher moiety selected from the group consisting of DABCYL, Reactive Red 4 (Cibacron Brilliant Red 3B-A), Malachite Green, 4-Dimethylaminophenylazophenyl-4'-isothiocyanate (DABITC), and 4,4'-Diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid moieties.

327. (Currently Amended) A method for enzymatically modifying a conjugate comprising the steps of:

providing a conjugate comprising a nucleic acid and a synthetic binding unit, wherein the synthetic binding unit is selected from the group consisting of pRNA, pDNA, and CNA, and wherein the nucleic acid and the synthetic binding unit are joined at a single attachment point; and

contacting the conjugate with at least one enzyme to effect modification of the nucleic acid, wherein when the synthetic binding unit is pRNA or pDNA, the synthetic binding unit and the nucleic acid are connected via a linkage selected from the group consisting of the 2' end of the synthetic binding unit to the 5' end of the nucleic acid, 2' end of the synthetic binding unit to the 3' end of the nucleic acid, 4' end of the synthetic binding unit to the 5' end of the nucleic acid, and 4' end of the synthetic binding unit to the 3' end of the nucleic acid.

328. (Previously Presented) The method of claim 327, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the other reagents include a nucleic acid which hybridizes to the NA of the conjugate.

329. (Previously Presented) The method of claim 327, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the other reagents include nucleoside triphosphates or modified nucleoside triphosphates.

330. (Previously Presented) The method of claim 327, wherein the at least one enzyme is selected from the group consisting of a polymerase, a ligase, an endonuclease, an exonuclease, a kinase, a methyltransferase, a methylase, a restriction endonuclease, and a terminal transferase.

331. (Previously Presented) The method of claim 327, wherein the at least one enzyme is a ligase, and the nucleic acid of the conjugate is modified by ligation of a terminus of the nucleic acid to at least one additional nucleic acid.

332. (Previously Presented) The method of claim 331, wherein the ligation is template-dependent, and wherein the nucleic acid of the conjugate and the at least one additional nucleic acid are hybridized to adjacent sequences of a template nucleic acid.

333. (Previously Presented) The method of claim 331, wherein the ligation is template-independent, and wherein the nucleic acid of the conjugate and the at least one additional nucleic acid are single stranded.

334. (Previously Presented) The method of claim 333, wherein the ligase used is a T4 RNA ligase.

335. (Previously Presented) The method of claim 331, wherein the ligation is a blunt-end, and wherein the nucleic acid of the conjugate and the at least one additional nucleic acid are double stranded.

336. (Previously Presented) The method of claim 327, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a polymerase, wherein the nucleic acid of the conjugate has an unblocked 3' terminus, wherein the other reagents comprise a template nucleic acid to which the unblocked 3' terminus of the nucleic acid hybridizes, and wherein the nucleic acid is modified by the addition of at least one nucleoside complementary to the template nucleic acid to the 3' terminus of the nucleic acid.

337. (Previously Presented) The method of claim 336, further comprising the step of adding a dideoxynucleotide to the nucleic acid of the conjugate.

338. (Previously Presented) The method of claim 336, further comprising the step of adding a labeled nucleotide to the nucleic acid of the conjugate.

339. (Previously Presented) The method of claim 336, wherein the template nucleic acid is derived from a biological sample.

340. (Previously Presented) The method of claim 339, wherein the biological sample is derived from a sample selected from the group consisting of human materials, animal materials, plant materials, fungal materials, cell cultures, viral cultures, food samples, and water samples.

341. (Previously Presented) The method of claim 336, wherein the polymerase is at least one enzyme selected from the group consisting of DNA polymerases, RNA polymerases, and reverse transcriptases.

342. (Previously Presented) The method of claim 336, wherein at least a portion of the template nucleic acid sequence is amplified.

343. (Previously Presented) The method of claim 336, wherein the polymerase is a thermostable polymerase, and wherein the step of contacting the conjugate with at least one enzyme comprise thermocycling the conjugate and the at least one enzyme to alternately i) dissociate extension products from the template nucleic acid and ii) allow the hybridization of conjugate nucleic acid to the template and enzymatic extension of the nucleic acid of the conjugate, wherein at least a portion of the template nucleic acid sequence is amplified.

344. (Previously Presented) The method of claim 336, further comprising contacting the conjugate with a restriction endonuclease, wherein the nucleic acid of the conjugate comprises an endonuclease recognition sequence 5' of the 3' terminus which hybridizes to the template nucleic acid, and wherein at least a portion of the template nucleic acid sequence is amplified by strand displacement amplification.

345. (Previously Presented) The method of claim 336, wherein the polymerase is a mixture of an RNA polymerase and a reverse transcriptase, further comprising contacting the conjugate with a RNAase H enzyme, wherein at least a portion of the template nucleic acid sequence is amplified by transcription mediated amplification.

346. (Previously Presented) The method of claim 327, wherein the enzyme is a terminal transferase, and the nucleic acid of the conjugate is modified by addition of at least one nucleoside to the 3' terminus of the nucleic acid.

347. (Previously Presented) The method of claim 346, further comprising the step of adding a labeled nucleoside to the nucleic acid of the conjugate.

348. (Previously Presented) The method of claim 346, wherein a homopolymeric tail is added to the nucleic acid of the conjugate.

349. (Previously Presented) The method of claim 327, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the nucleic acid of the conjugate and the target nucleic acid are cleaved by the restriction endonuclease.

350. (Previously Presented) The method of claim 327, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the nucleic acid of the conjugate but not the target nucleic acid is cleaved by the restriction endonuclease.

351. (Previously Presented) The method of claim 327, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the at least one enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the target nucleic acid but not the nucleic acid of the conjugate is cleaved by the restriction endonuclease.

352. (Previously Presented) The method of claim 327, further comprising contacting the conjugate and at least one enzyme with other reagents, wherein the enzyme is a RNAse H, wherein the other reagents comprise an RNA target nucleic acid to which at least a portion of the nucleic acid of the conjugate hybridizes, and wherein the target RNA nucleic acid hybridizing to the nucleic acid of the conjugate is degraded by the RNAse H.

353. (Previously Presented) The method of claim 327, wherein the enzymatic modification is within 30 nucleotides of the attachment point.

354. (Previously Presented) The method of claim 327, wherein the enzymatic modification is within 20 nucleotides of the single attachment point.

355. (Previously Presented) The method of claim 327, wherein the enzymatic modification is within 15 nucleotides of the single attachment point.

356. (Previously Presented) The method of claim 327, wherein the enzymatic modification is within 10 nucleotides of the single attachment point.

357. (Previously Presented) The method of claim 327, wherein the enzymatic modification is within 7 nucleotides of the single attachment point.

358. (Previously Presented) The method of claim 327, wherein the enzymatic modification is within 5 nucleotides of the single attachment point.

359. (Previously Presented) The method of claim 327, wherein the enzymatic modification is within 2 nucleotides of the single attachment point.

360. (Previously Presented) The method of claim 327, wherein the enzymatic modification is the nucleotide at the single attachment point.

361-364. (Canceled)

365. (Previously Presented) The method of claim 327, wherein the nucleic acid is selected from the group consisting of deoxyribonucleic acids, ribonucleic acids, and chemically modified nucleic acids.

366. (Previously Presented) The method of claim 327, wherein the nucleic acid is selected from the group consisting of phosphorothioate nucleic acids, phosphorodithioate nucleic acids, methylphosphonate nucleic acids, 2'-O-methyl RNA, and 2'-fluoro RNA.

367. (Previously Presented) The method of claim 327, wherein the nucleic acid is selected from the group consisting of peptide nucleic acids (PNA) and locked nucleic acids (LNA.)

368. (Previously Presented) The method of claim 327, wherein the nucleic acid is selected from the group consisting of an aptamer and an aptazyme.

369. (Previously Presented) The method of claim 327, wherein the conjugate further comprises at least one labeling moiety.

370. (Previously Presented) The method of claim 369, wherein the at least one labeling moiety is selected from the group consisting of fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, micro-particles, paramagnetic micro-particles, and enzymatic labeling moieties.

371. (Previously Presented) The method of claim 369, wherein the labeling moiety is a fluorescent dye moiety selected from the group consisting of: boron dipyrromethane difluoride dyes, cyanine dyes, fluorescein dyes, rhodamine dyes, phycoerythrin dyes, coumarin dyes, Texas Red dyes, green dyes, FAM, HEX, TET, TAMRA, ROX, EDANA, 4-Acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid, 4,4'-Diisothiocyanatostilbene-2,2'-disulfonic acid, Succinimidyl pyrene butyrate, Acridine isothiocyanate, Cascade Blue, Oregon Green, Lucifer Yellow vinyl sulfone, and IR1446.

372. (Previously Presented) The method of claim 369, wherein the labeling moiety is a quencher moiety selected from the group consisting of DABCYL, Reactive Red 4 (Cibacron Brilliant Red 3B-A), Malachite Green, 4-Dimethylaminophenylazophenyl-4'-isothiocyanate (DABITC), and 4,4'-Diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid moieties.